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$Gd@C_{82}$ metallofullerenes for neutron capture therapy—fullerene solubilization by poly(ethylene glycol)-block-poly(2-(*N*,*N*-diethylamino)ethyl methacrylate) and resultant efficacy *in vitro*

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Abstract
Poly(ethylene glycol)-block-poly(2-(*N*,*N*-diethylamino)ethyl methacrylate) (PEG-*b*-PAMA) was found to solubilize fullerenes such as C_{60}, and this technique was applied to metallofullerenes. $Gd@C_{82}$ was easily dissolved in water in the presence of PEG-*b*-PAMA without any covalent derivatization, forming a transparent complex about 20–30 nm in diameter. Low cytotoxicity was confirmed *in vitro*. Neutron irradiation of cultured cells (colon-26 adenocarcinoma) with $Gd@C_{82}$-PEG-*b*-PAMA-complexed nanoparticles showed effective cytotoxicity, indicating the effective emission of gamma rays and internal conversion electrons produced from the neutron capture reaction of Gd. This result suggests a potentially valuable approach to gadolinium-based neutron capture therapy.

Keywords: neutron capture therapy, GdNCT, fullerene, $Gd@C_{82}$, PEG-*b*-polyamine, *in vitro*

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1. Introduction

Neutron capture therapy (NCT) is a suitable method for the treatment of intractable tumors such as brain tumors. NCT using ^{10}B (BNCT) has demonstrated efficacy in the treatment of tumors [1, 2] and is now established as a frontier radiotherapy. ^{10}B compounds based on boronophenylalanine (BPA) and sodium borocaptate (BSH) have undergone clinical trials to verify their efficacy in BNCT because they show low cytotoxicity without neutron irradiation [3–5]. However, since selective accumulation in tumors is insufficient, improvements in targeting characteristics are desirable. We have recently developed boron-containing nanoparticles for passive targeting in tumors, which improves the BNCT efficiency. Another important requirement for high-performance neutron therapy is the monitoring of the biodistribution of compounds, including neutron capture agents. Precise determinations of the capture compound concentration would facilitate minimization of the neutron source power and reduce damage to normal organs by neutron irradiation.

Gadolinium is a promising candidate for monitoring biodistribution by magnetic resonance imaging (MRI)

